Attorney Docket No. PC10228A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Farzan Rastinejad et al. :

APPLICATION NO.: 09/443,542 : Examiner: Gregory W. Mitchell

FILING DATE: November 19, 1999 : Group Art Unit: 1617

TITLE: METHODS AND COMPOSITIONS FOR RESTORING CONFORMATIONAL STABILITY OF A PROTEIN OF THE p53 FAMILY :

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Inventor Declaration under 37 CFR 1.132

I, Dr. Farzan Rastinejad, an inventor on the above-identified application, make this declaration in support thereof.

I received my Ph.D. degree from Northwestern University, Chicago, Illinois, in 1988. For the last eleven (11) years, I have been employed by Pfizer, Inc. where I am Senior Principal Investigator for Oncology.

The attached data printout sheets show the results of testing (according to the general protocol of Example 1 of the present application) of compounds to determine their efficacy in stabilizing the native conformation of p53. In Panel I of the printout (Pages1-9), the "SC50" value ("stabilizing concentration") represents the concentration of the test compound (usually micromolar, unless the compound is reported as inactive or weekly inactive) needed to retain (per the Example 1 protocol) 50% of maximal binding of a p53-specific antibody whose binding to p53 is conformationally dependent (for non denatured p53). The periods of incubation vary somewhat, since the data was intended to be qualitative, useful for a broad comparison, but are generally about 30 minutes at about 37 degrees C.

The data evidence a wide variety of chemical compounds that bind to p53 and can stabilize it, including many as disclosed in the above-identified patent application. The data panels show a complete listing of all compounds tested in the panel, including large umbers of compounds that are not effective in the practice of the invention. Similarly, Panel 2 of the printout (the subsequently following Pages 1-33) shows additional compounds having activity according to the practice of the invention (again as measured by SC50, data in far right column), and the inactive compounds of this subsequent panel are also shown. The lack of a number in the far right hand column means that the compound was inactive.

I acknowledge that all statements made of my own knowledge, are true and that all statements made on information and belief are believed to be true.

I further acknowledge that willful false statements, and the like, are punishable by fine or imprisonment, or both (18 USC section 1001) and may jeopardize the validity of the application or any patents issuing thereon.

Dated: _____ _____

Dr. Farzan Rastinejad

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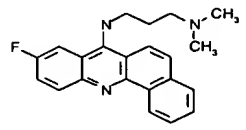
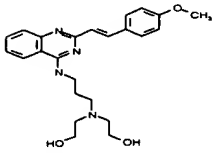
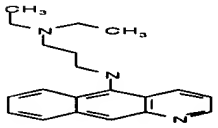
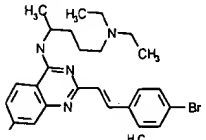
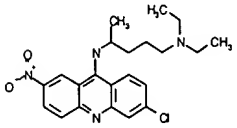
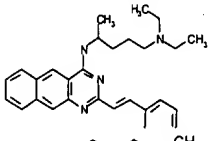
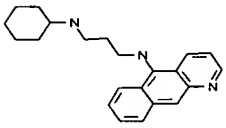
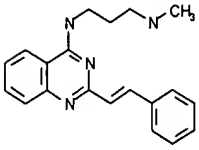
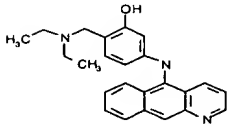
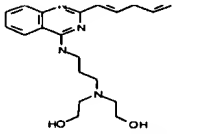
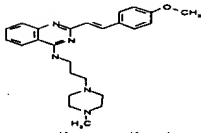
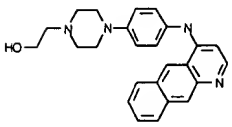
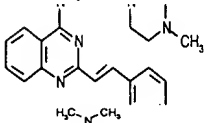
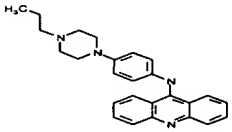
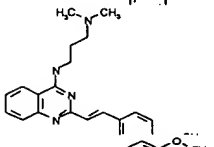
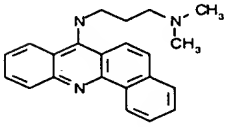
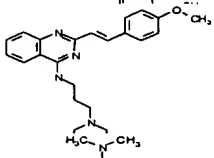
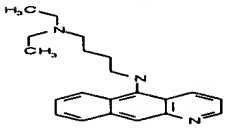
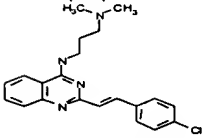
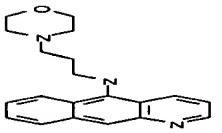
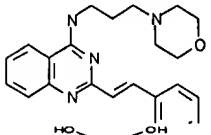
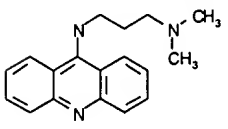
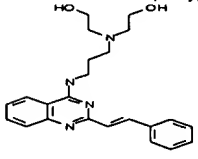
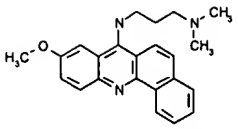
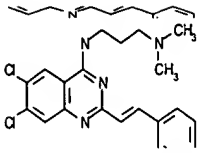
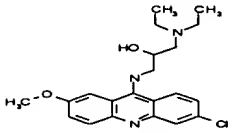
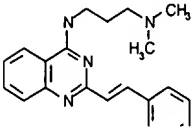
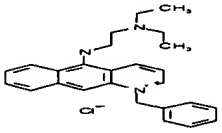
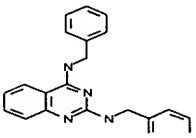
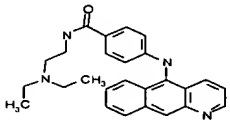
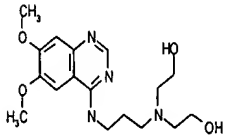
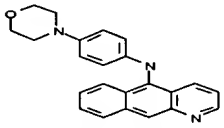
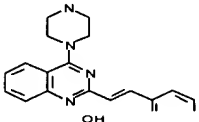
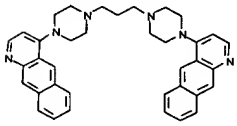
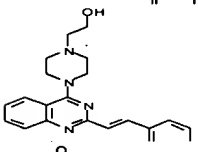
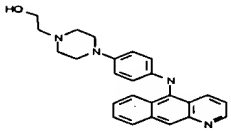
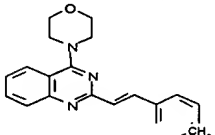
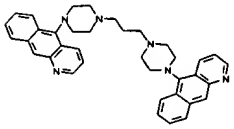
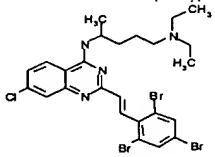
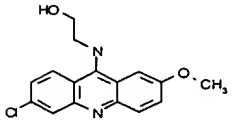
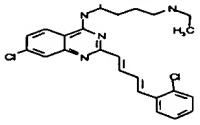
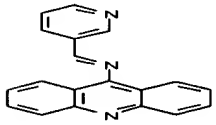
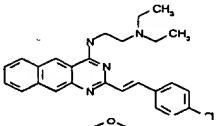
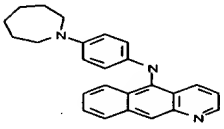
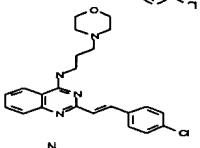
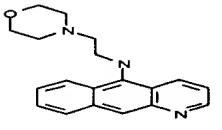
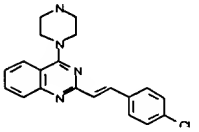
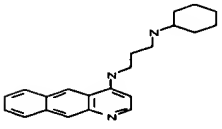
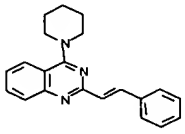
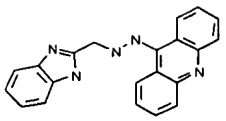
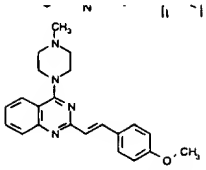
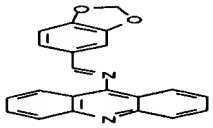
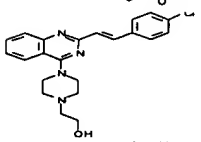
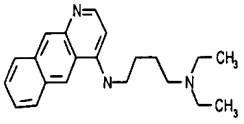
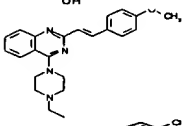
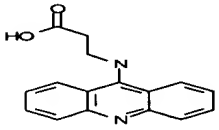
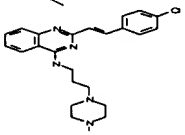
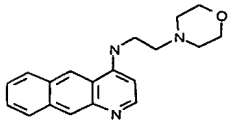
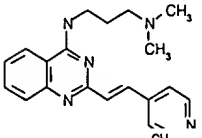
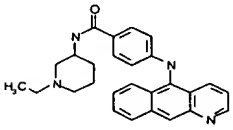
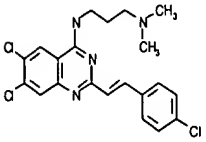
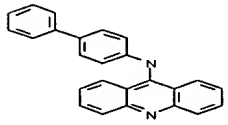
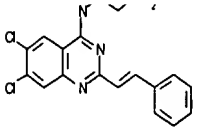
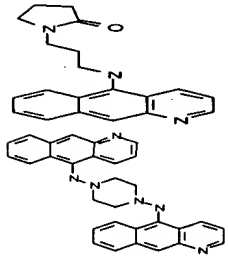
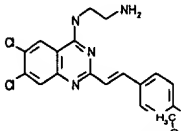
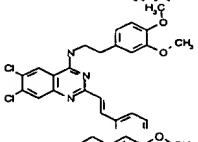
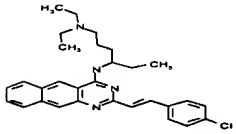
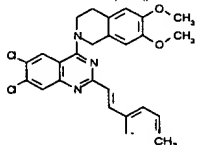
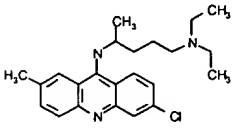
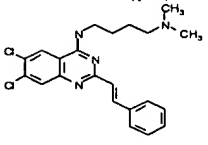
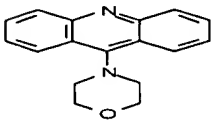
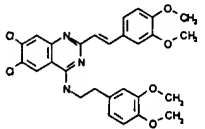
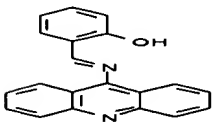
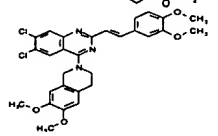
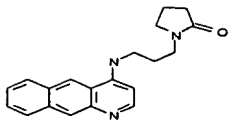
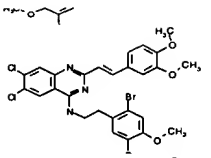
	7		7
	50		9
	53		10
	54		13
	59		16
			17
	100		19
	100		23
	120		23
	120		32
	120		36
	150		36

	180		57
	220		94
	220		WEAK
	240		INACTIVE
	280		INACTIVE
	WEAK(300)		INACTIVE
	WEAK(430)		INACTIVE
	WEAK		WEAK
	WEAK		WEAK
	WEAK		WEAK
	WEAK		WEAK
	WEAK		WEAK
	WEAK		INACTIVE

	INACTIVE		WEAK
	INACTIVE		INACTIVE
	WEAK		WEAK
	WEAK		WEAK
	INACTIVE		WEAK(750
	INACTIVE		WEAK
	INACTIVE		WEAK
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	WEAK		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE

	WEAK-IN	
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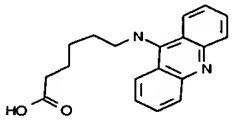
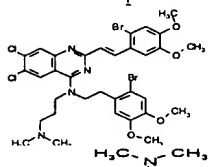
	WEAK-IN	
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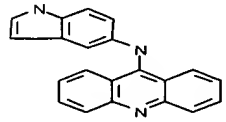
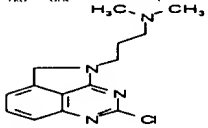
	WEAK-IN	
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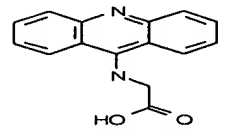
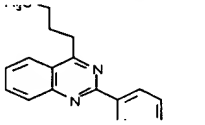
	WEAK-IN	
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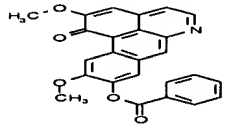
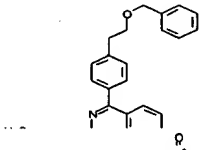
	WEAK-IN	
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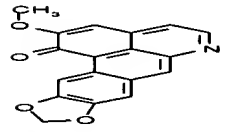
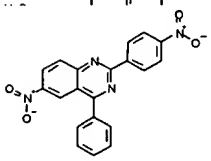
	WEAK-IN	
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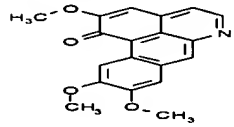
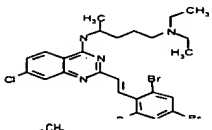
	WEAK-IN	
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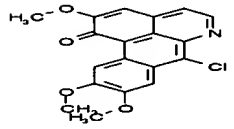
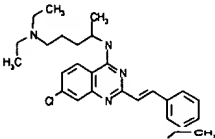
	WEAK-IN	
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		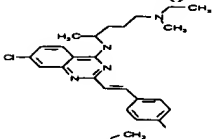
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		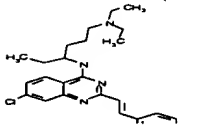
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		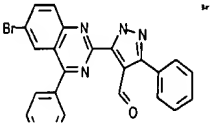
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		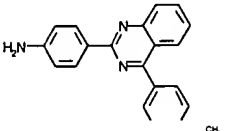
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		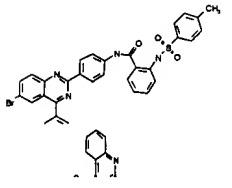
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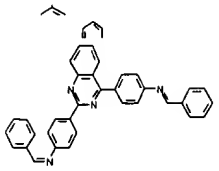

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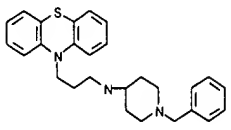
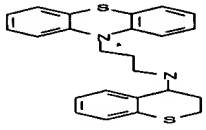
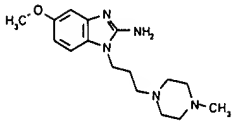
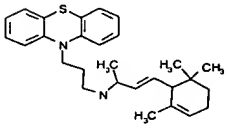
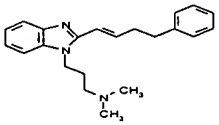
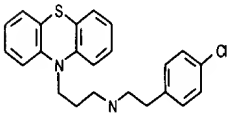
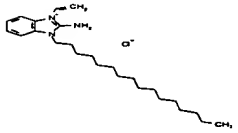
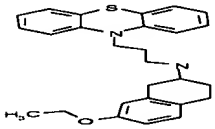
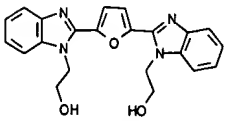
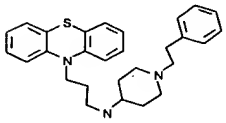
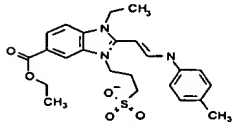
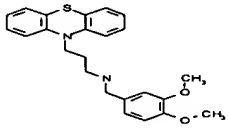
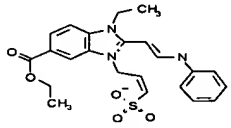
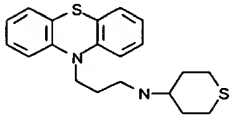
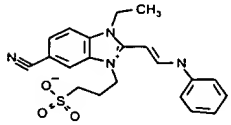
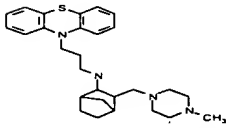
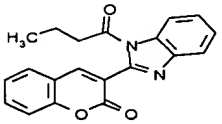
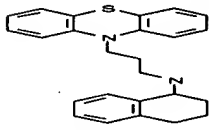
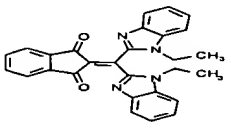
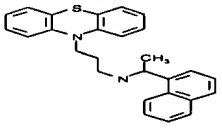
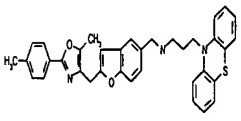
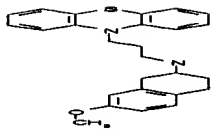
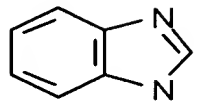
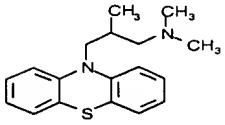
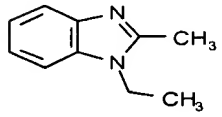
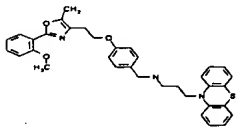
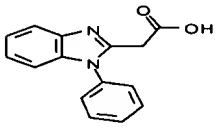
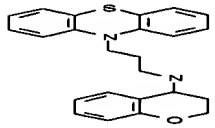
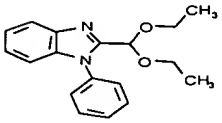
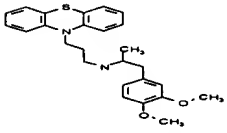
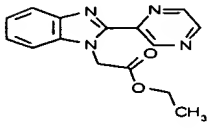
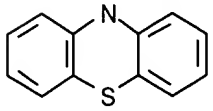
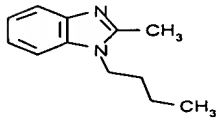
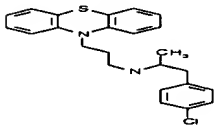
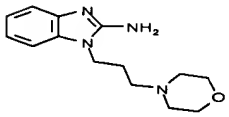
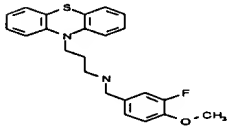
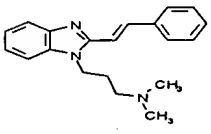
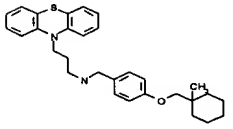
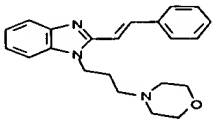
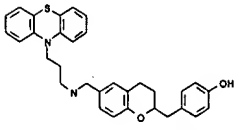
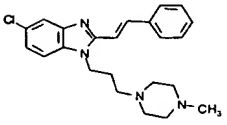
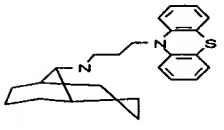
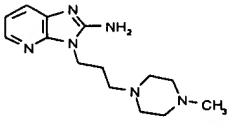
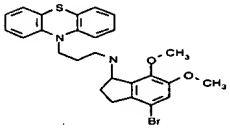
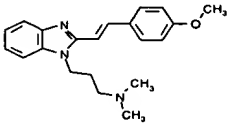
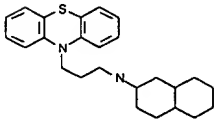
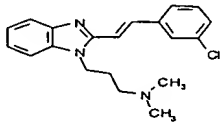
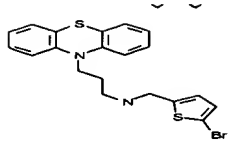
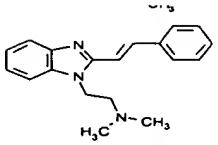
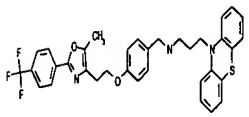
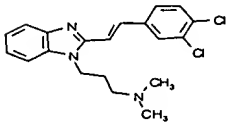
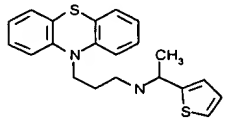
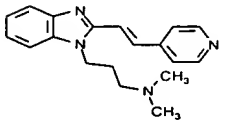
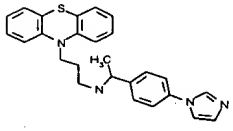
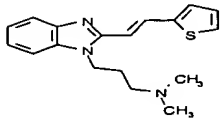
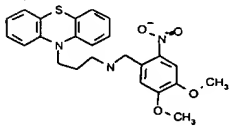
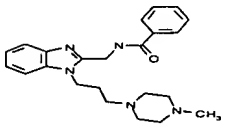
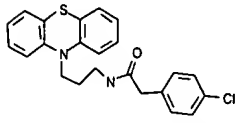
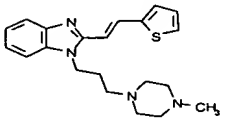
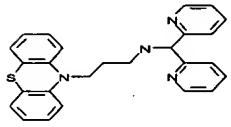
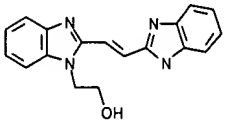
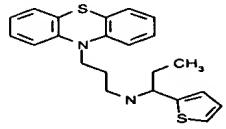
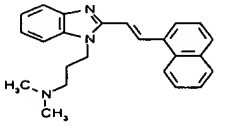
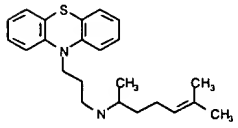
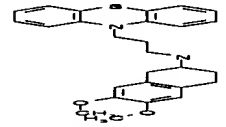
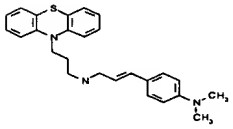
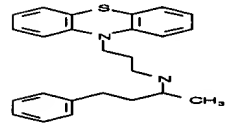
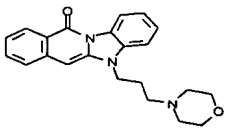
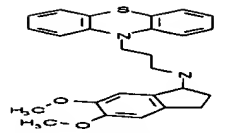
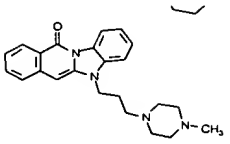
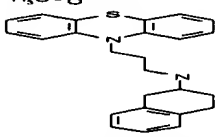
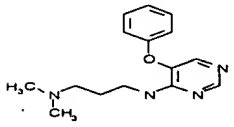
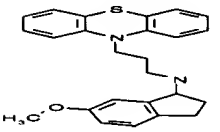
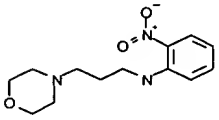
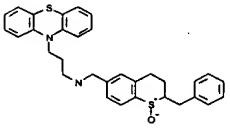
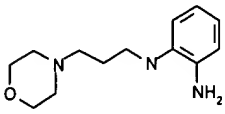
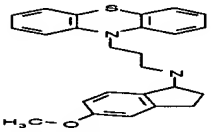
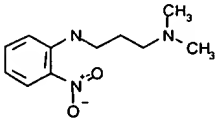
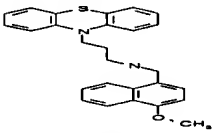
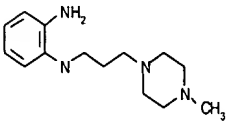
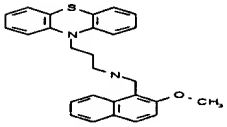
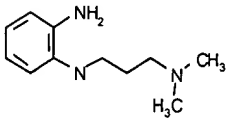
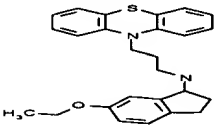
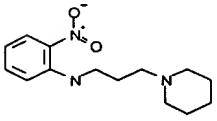
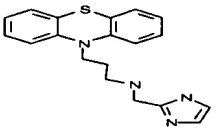
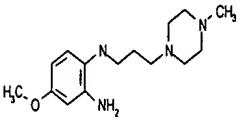
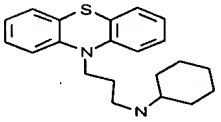
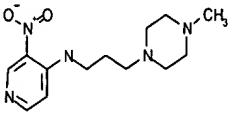
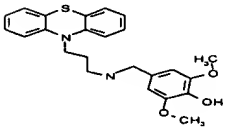
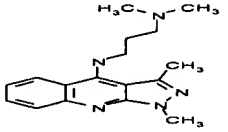
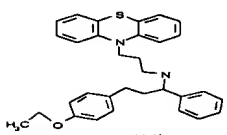
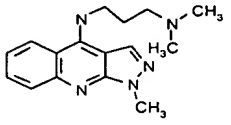
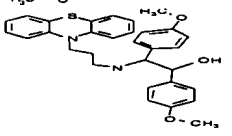
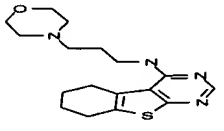
	4		
	5		130
	8		INACTIVE
	9		INACTIVE
	10		INACTIVE
	11		INACTIVE
	12		WEAK
	16		INACTIVE
	23		INACTIVE
	25		INACTIVE
	31		
	36		

	36		INACTIVE
	38		INACTIVE
	42		INACTIVE
	44		WEAK-IN.
	67		INACTIVE
	INACTIVE		INACTIVE
	WEAK		WEAK
	WEAK		INACTIVE
	INACTIVE		WEAK
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	WEAK-IN.		INACTIVE

	WEAK		INACTIVE
	INACTIVE		WEAK
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		
	INACTIVE		
	WEAK	MOLSTRUCTURE	SC50 (uM)
	WEAK		INACTIVE

	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	WEAK		INACTIVE
	WEAK		INACTIVE
	WEAK		INACTIVE
	INACTIVE		INACTIVE
	INACTIVE		INACTIVE
	WEAK-IN.		INACTIVE
	WEAK		INACTIVE
	INACTIVE		INACTIVE
	WEAK		INACTIVE

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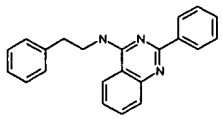
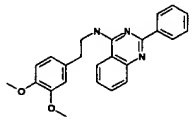
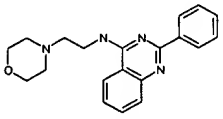
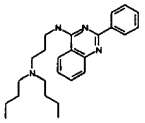
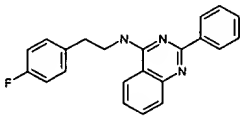
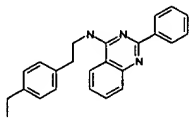
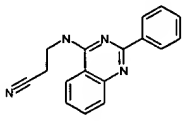
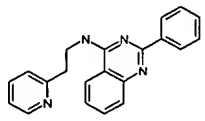
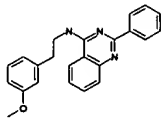
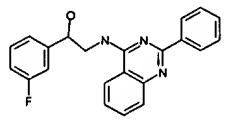
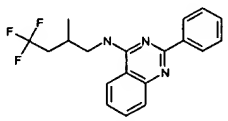
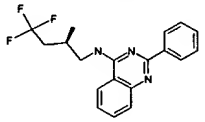
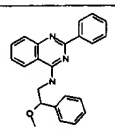
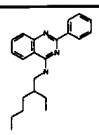
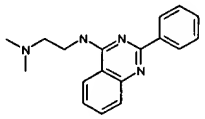
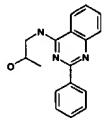
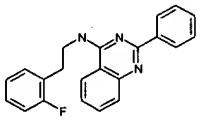
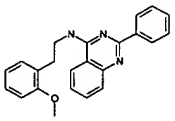
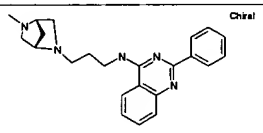
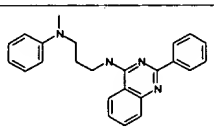
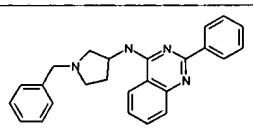
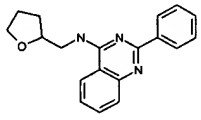
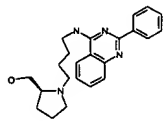
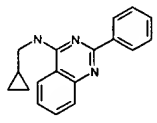
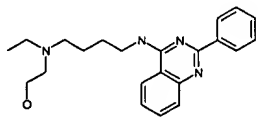
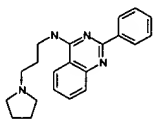
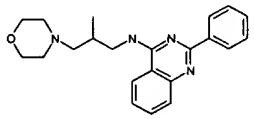
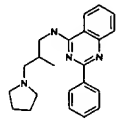
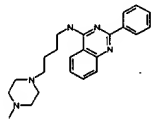
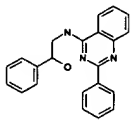
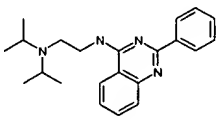
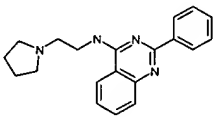
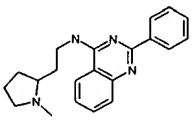
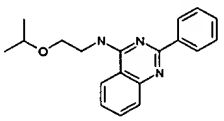
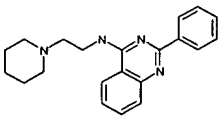
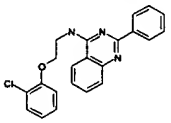
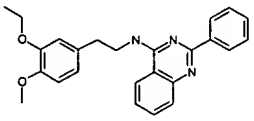
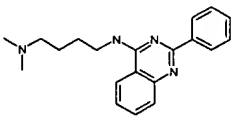
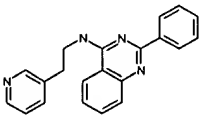
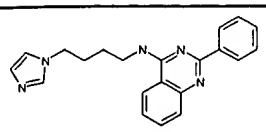
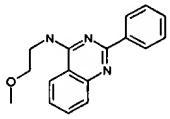
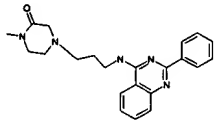
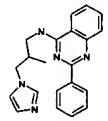
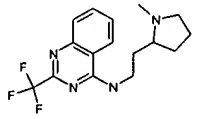
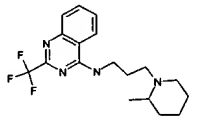
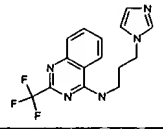
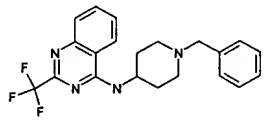
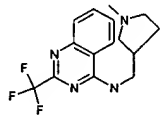
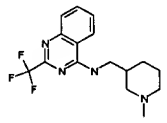
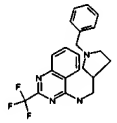
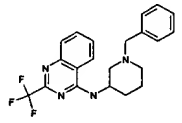
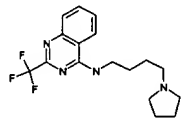
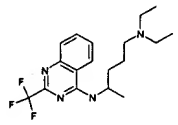
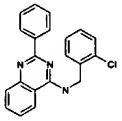
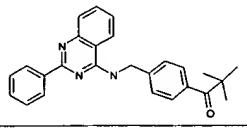
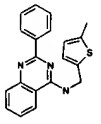
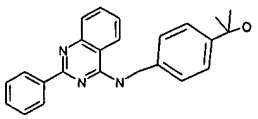
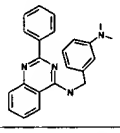
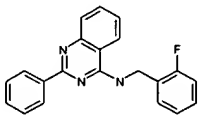
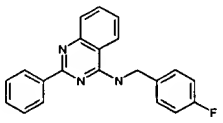
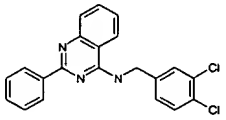
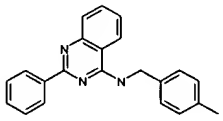
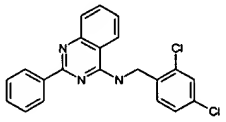
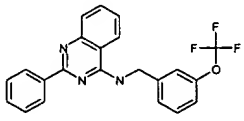
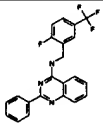
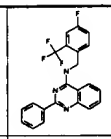
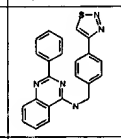
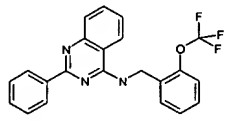
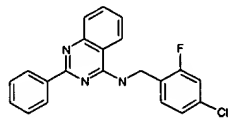
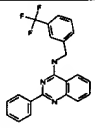
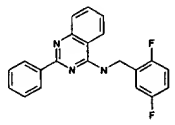
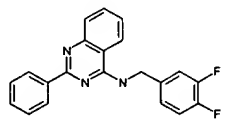
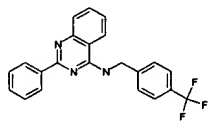
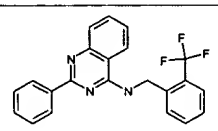
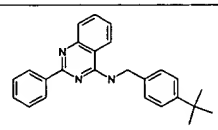
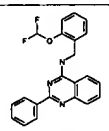
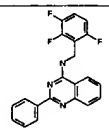
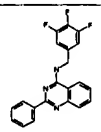
				
		X		
		X		
				
		X		
				
				
		X		
				
				
				
				
				

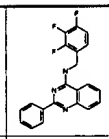
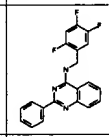
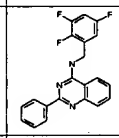
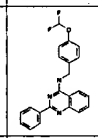
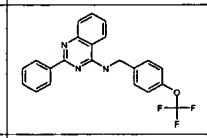
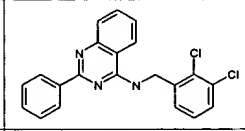
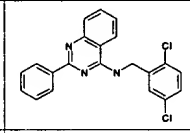
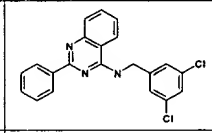
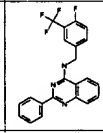
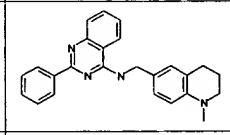
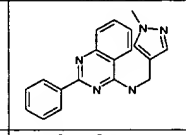
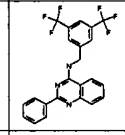
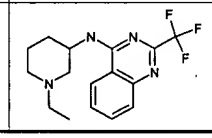
				
		X		
				
				
				
				
				
				
		X		
		X		
				
		X		
		X		

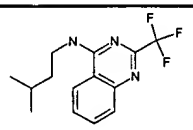
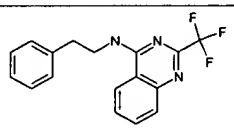
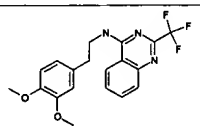
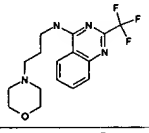
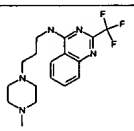
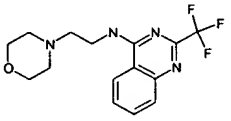
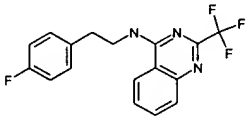
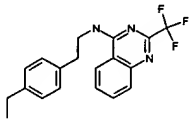
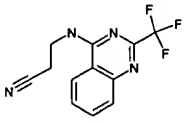
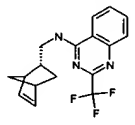
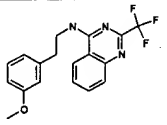
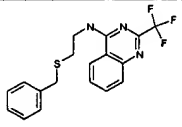
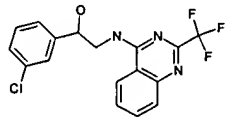
				
				
				30
		X		
				
				
				
		X		
		X		
				
		X		
		X		
				

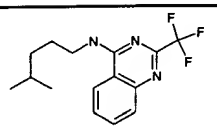
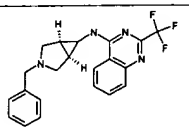
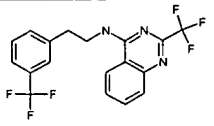
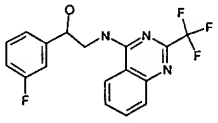
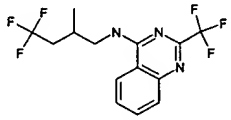
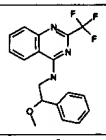
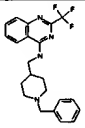
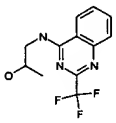
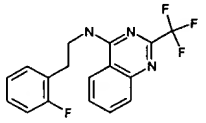
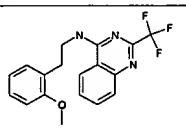
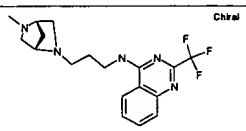
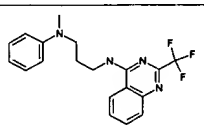
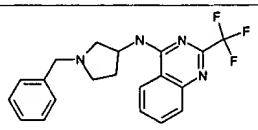
		X		
				
		X		
				
				
				
				
				
				
				
				
				
				

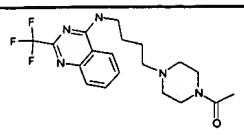
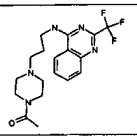
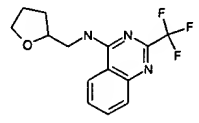
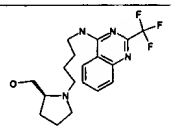
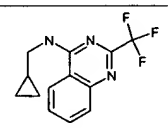
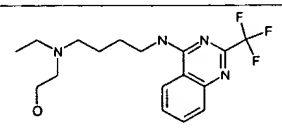
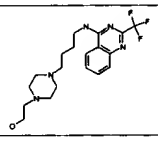
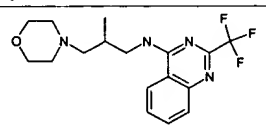
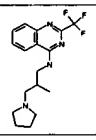
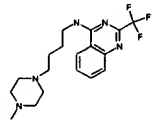
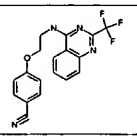
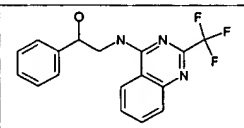
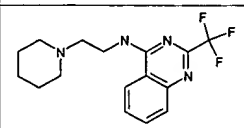
				
				
				
				
				
				
				
				
		X		
				
				
				
				

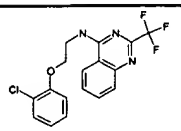
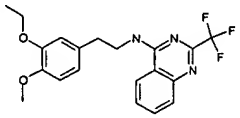
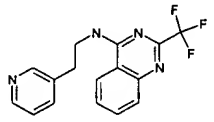
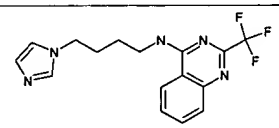
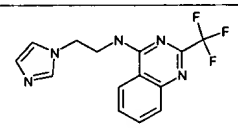
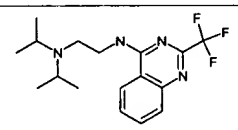
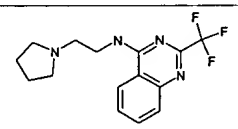
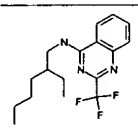
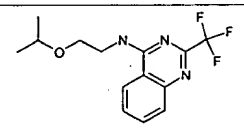
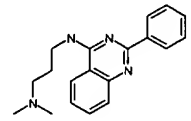
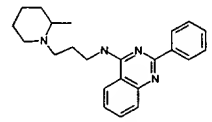
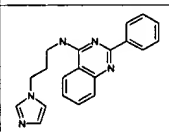
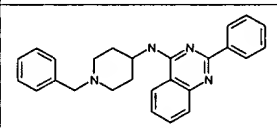
				
				
				
				
				
				
				
				
				
				
				
				
				

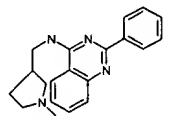
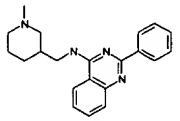
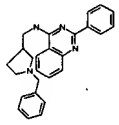
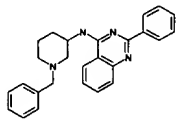
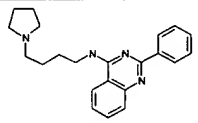
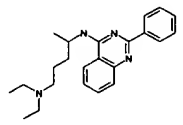
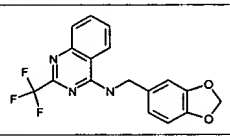
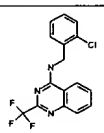
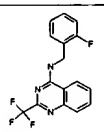
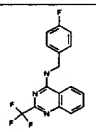
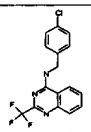
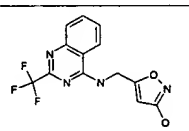
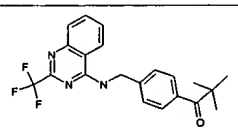
				
				
				
				
				
				
				
				
				
				
				
				
				

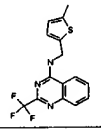
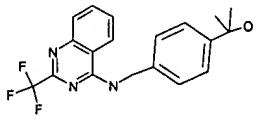
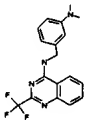
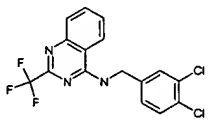
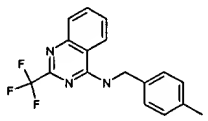
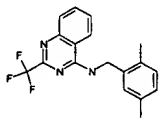
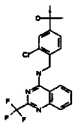
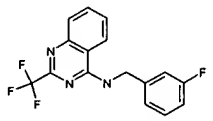
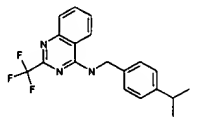
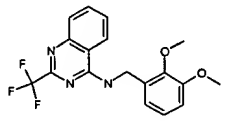
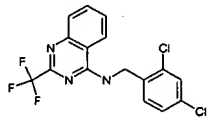
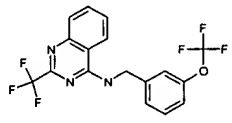
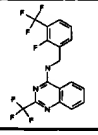
				
				
				
				
				
		X		
				
				
				
				
				
				
				

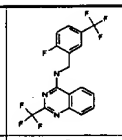
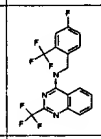
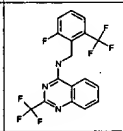
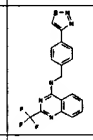
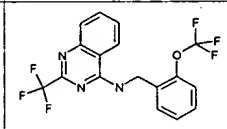
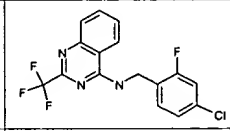
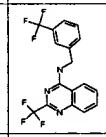
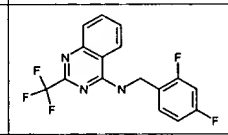
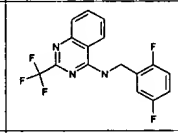
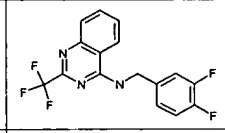
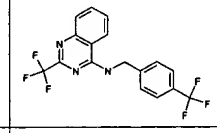
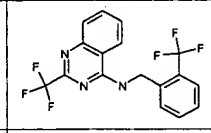
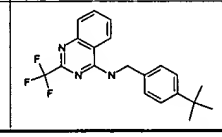
				
				
				
				
				
				
				
				
				
				
	 Chiral			
				
				

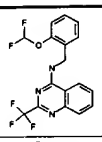
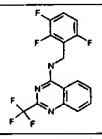
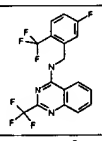
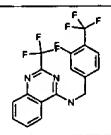
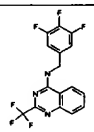
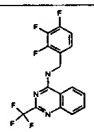
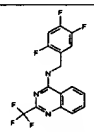
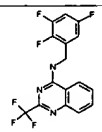
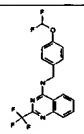
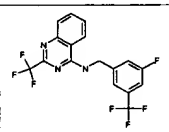
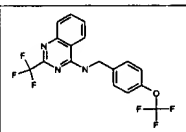
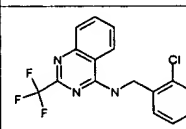
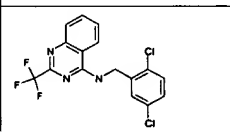
				
				
				
				
				
	 X			
				
				
				
				
				
				
				

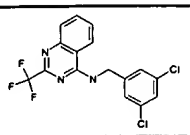
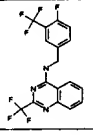
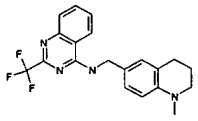
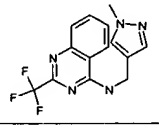
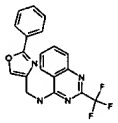
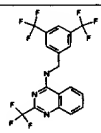
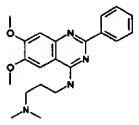
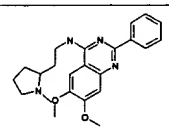
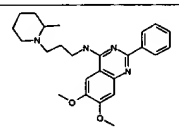
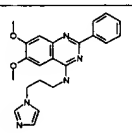
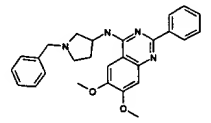
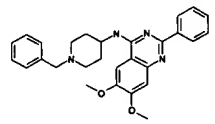
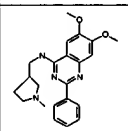
				
				
				
				
		X		
				
				
				
				
		X		
				
				
				

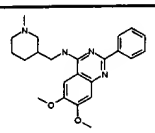
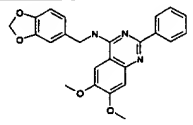
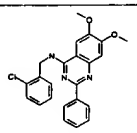
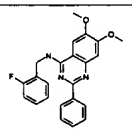
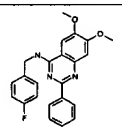
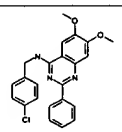
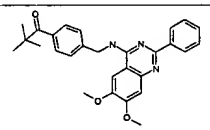
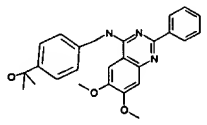
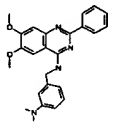
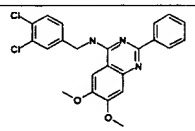
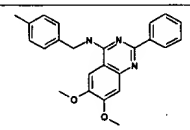
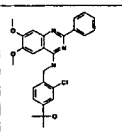
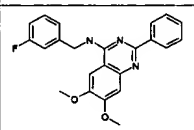
				
				
				
				
				
				
				
				
				
				
				
				
				

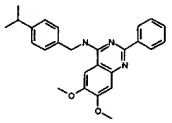
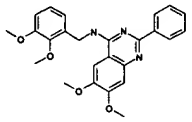
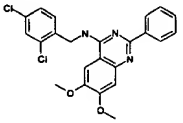
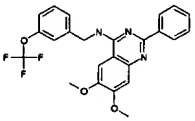
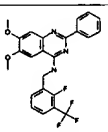
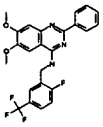
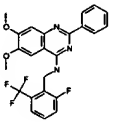
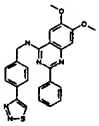
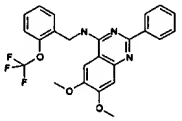
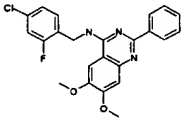
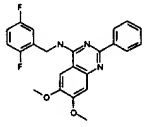
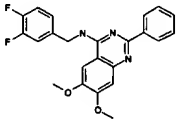
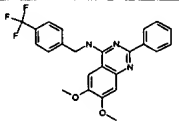
				
				
				
		X		
				
				
				
				
				
				
				
				
				

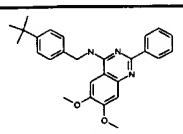
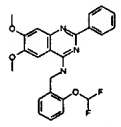
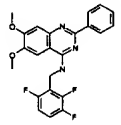
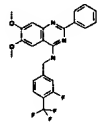
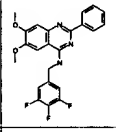
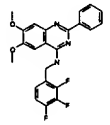
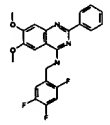
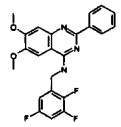
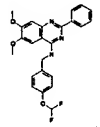
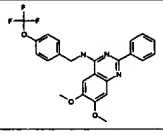
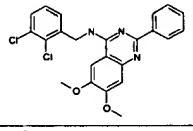
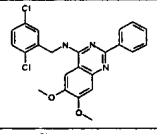
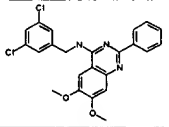
				
				
				
				
				
				
				
				
				
				
				
				
				

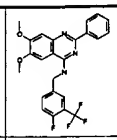
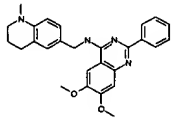
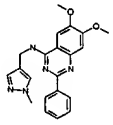
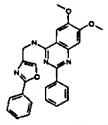
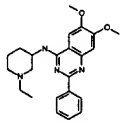
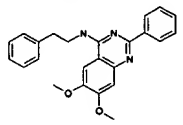
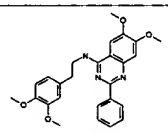
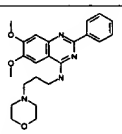
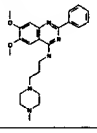
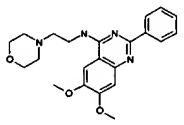
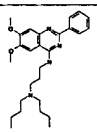
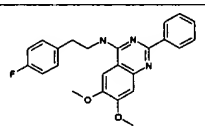
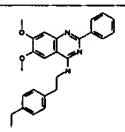
				
				
				
				
				
				
				
				
				
				
				
				
				

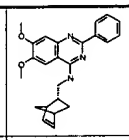
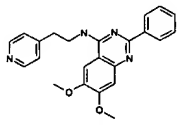
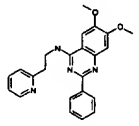
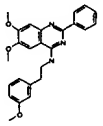
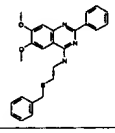
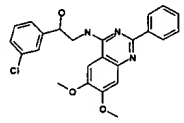
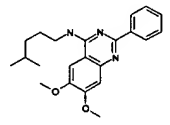
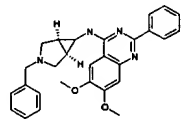
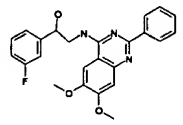
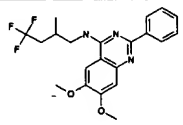
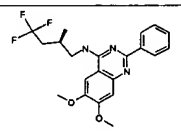
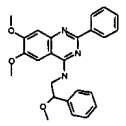
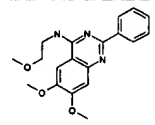
				
				
				
				
				
				
				
				
				
				
				
				
				

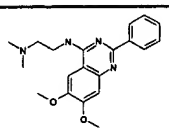
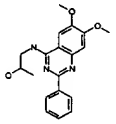
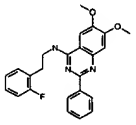
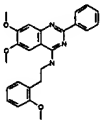
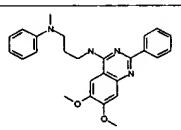
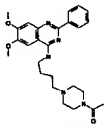
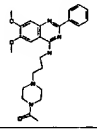
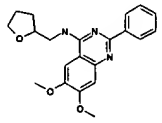
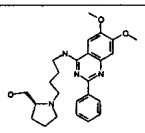
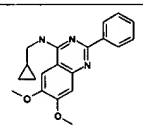
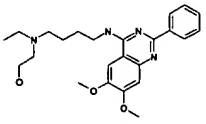
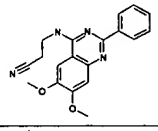
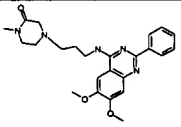
				
				
				
				
				
				
				
				
				
				
				
				
				

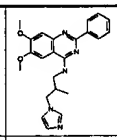
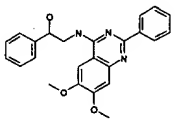
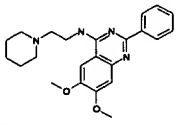
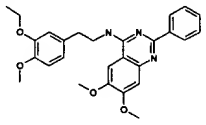
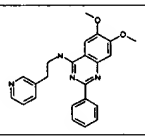
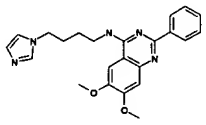
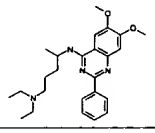
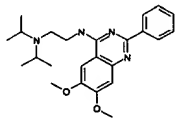
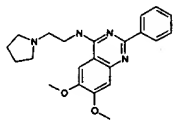
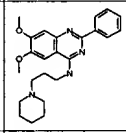
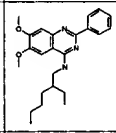
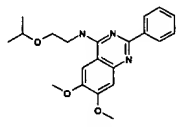
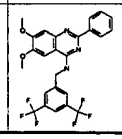
				
				
				
				
				
				
				
				
				
				
				
				
				

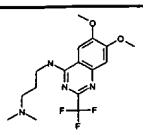
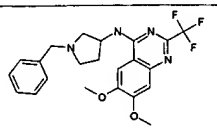
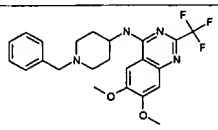
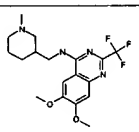
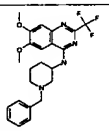
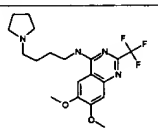
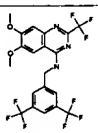
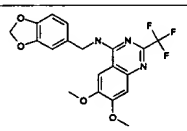
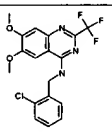
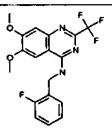
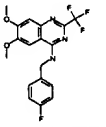
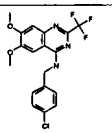
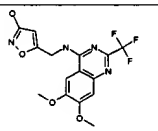
				
				
				
				
				
				
				
				
				
				
				
				
				

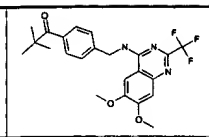
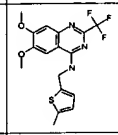
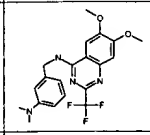
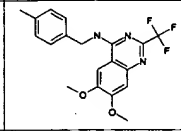
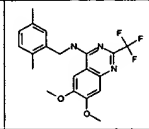
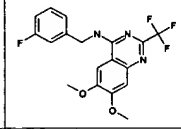
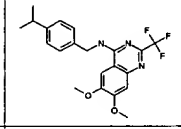
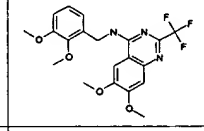
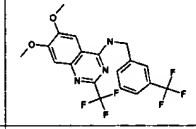
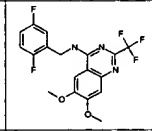
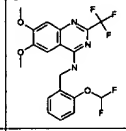
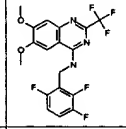
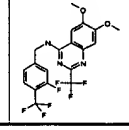
				
				
				
				
				
				
				
				
				22
				
				
				
				

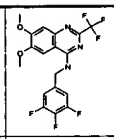
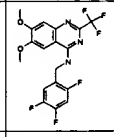
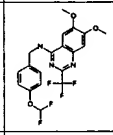
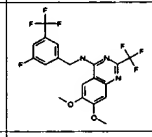
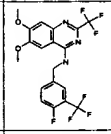
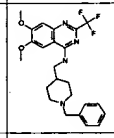
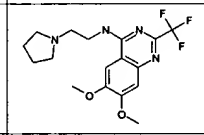
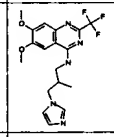
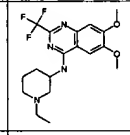
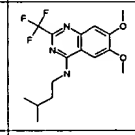
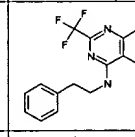
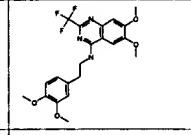
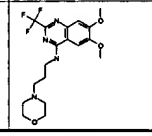
				
				
				
				
				
				
				
				
				
				
				
				
				

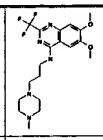
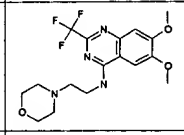
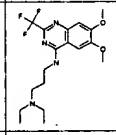
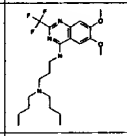
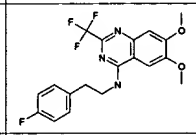
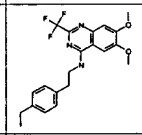
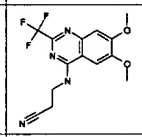
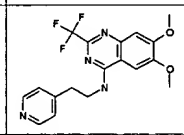
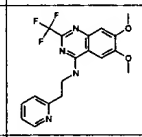
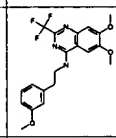
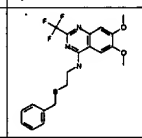
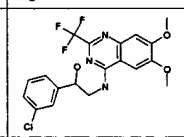
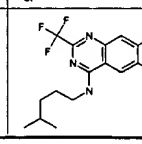
		X		
				
				
				
				
				52
				
				
				50
				
		X		22
				
				

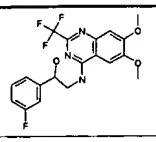
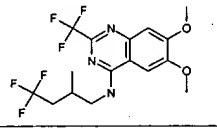
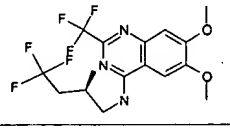
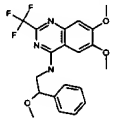
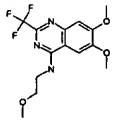
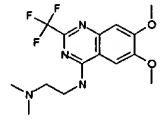
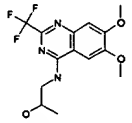
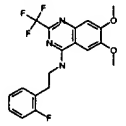
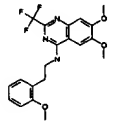
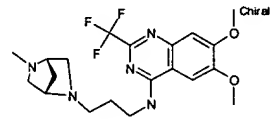
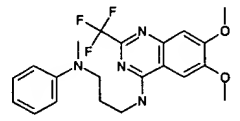
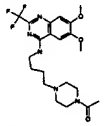
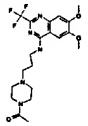
				
				
				
				
				
		X		
				
				
		X		
				50
				
				
				

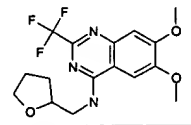
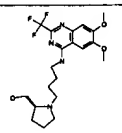
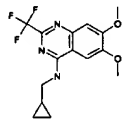
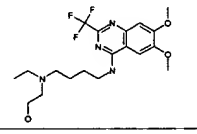
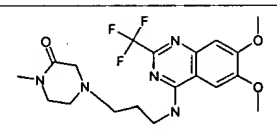
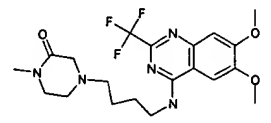
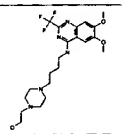
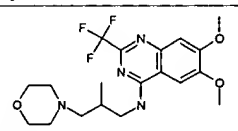
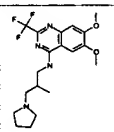
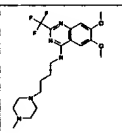
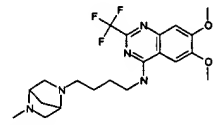
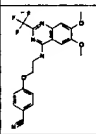
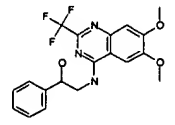
				
				
				
				
				
				
				
				
				
				
				
				
				

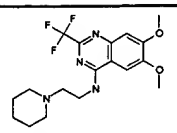
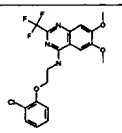
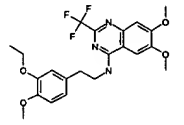
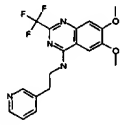
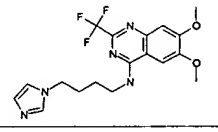
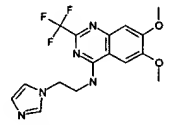
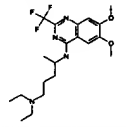
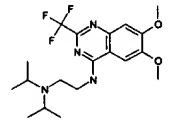
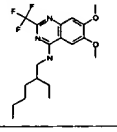
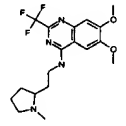
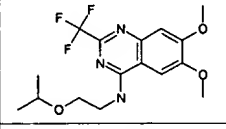
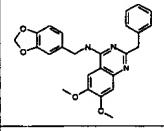
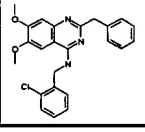
				
				
				
				
				
				
				
				
				
				
				
				
				

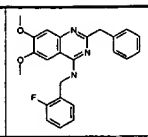
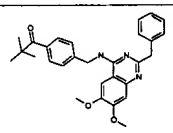
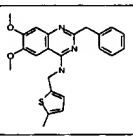
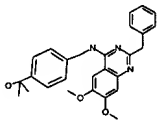
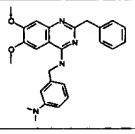
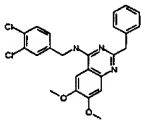
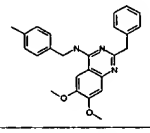
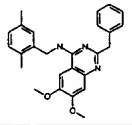
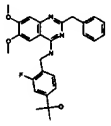
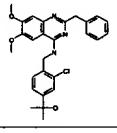
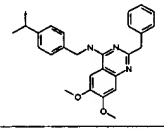
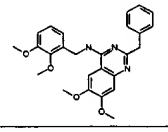
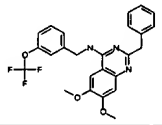
				
				
				
				
				
				60
				
				
				
				
				
				
				

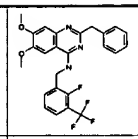
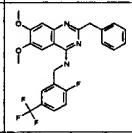
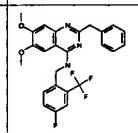
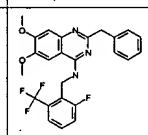
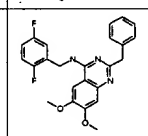
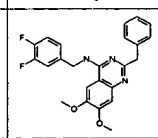
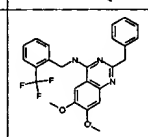
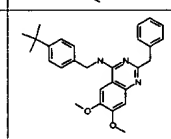
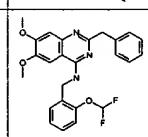
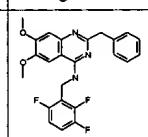
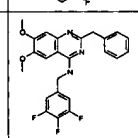
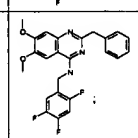
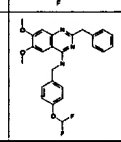
				
				
				
				
				
				
				
				
				
				
				
				
				

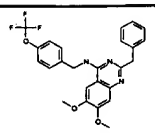
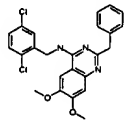
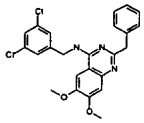
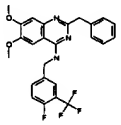
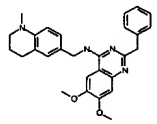
				
				
				
				
				
				
				
				
				
	 Chiral			
				
				
				

				
				
				
				
				55